

REMARKS

Claims 1-25 and 68 were canceled previously without prejudice to, or disclaimer of, the subject matter recited therein. The Examiner previously withdrew claims 51-67 from consideration. In the present amendment, applicants cancel claims 51-67 without prejudice to, or disclaimer of, the subject matter recited therein. Applicants expressly reserve the right to pursue the subject matter of any of the canceled claims in a related application in the future.

Claim 26 has been amended to include the language "the first reaction composition comprises amplification primers specific to the at least one target polynucleotide and lacks a fluorescent indicator," in accordance with the Examiners' suggestion provided during an interview with the undersigned on March 6, 2007 (see Interview Summary below). Support for that amendment is found in the specification, for example, at page 14, paragraph [042], which states that "[i]n certain embodiments, one does not actually sequence the amplification product from the reaction composition that includes the fluorescent indicator." Thus, that amendment adds no new matter. Furthermore, that amendment raises no new issues requiring further examination. Claims 26-50 are under consideration.

I. Applicants Statement of Interview Summary

The undersigned thanks Examiner Tung and Primary Examiner Horlick for the courtesy of the telephone interview on March 6, 2007. The Examiners and the undersigned discussed the claim rejections in view of Wittwer.

Specifically, the undersigned pointed out that independent claim 26 recites multiple elements. The undersigned also pointed out that, in previous responses filed at the U.S. Patent and Trademark Office on June 22, 2006, November 14, 2006, and January 16, 2007, ("previous responses"), Applicants asserted that Wittwer does not teach or suggest, either expressly or inherently, each and every element of independent claim 26. Specifically, the undersigned stated that in the previous responses, Applicants asserted that Wittwer does not teach or suggest at least the claim language "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition . . . , " according to the method of claim 26.

The undersigned also asserted that Wittwer does not meet the standard for inherent anticipation because that document does not "make clear that the missing descriptive matter is necessarily present." As explained in the Response filed on January 16, 2007, in Wittwer, each reaction composition comprises a fluorescent indicator and the fluorescence in each reaction composition is determined. Response filed January 16, 2007, at page 5. "It is clear, then, that Wittwer requires detection of the fluorescent signal in the same reaction composition as that containing the target

nucleic acid.” *Id.* Thus, one of the reaction compositions would not have been used to detect the target nucleic acid in another reaction composition. *Id.* Accordingly, “Wittwer does not teach or suggest, either expressly or inherently, ‘determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition,’ according to the method of claim 26.” *Id.* at pages 5 to 6.

During the interview, Examiner Horlick acknowledged that the “intended invention” is free of Wittwer but expressed his view that the distinction is not clear from the claim language. Examiner Horlick and the undersigned discussed possible clarifying amendments to claim 26, including the amendment presented in this paper.

Below, Applicants address the rejections.

II. Rejection of Claims 26, 28-35, 39, 40, 43-45, and 47-50 Under 35 U.S.C. § 102(e)

The Examiner maintained the rejection of claims 26, 28-35, 39, 40, 43-45, and 47-50 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,174,670 (“Wittwer”). Action at page 2, item no. 1. Applicants respectfully traverse that rejection.

The Examiner alleged that “Wittwer et al. disclose the method of monitoring hybridization during polymerase chain reaction using of double stranded DNA dye or specific hybridization probes and quantitating amplified DNA. . . .” Action at page 2. The Examiner acknowledged that

Wittwer et al. do not explicitly disclose combining nucleic acid from the sample with at least one set of reaction composition comprising a first reaction composition and second reaction composition, both specific for the at least one target polynucleotide, wherein the first reaction composition comprises amplification primers specific to at least one target polynucleotide and the second reaction composition comprises a fluorescent indicator and amplification primers specific to at least one target polynucleotide.

Id. at page 3.

But the Examiner alleged that

Wittwer et al. disclose that three fluorescence-monitoring techniques for PCR are performed. Each reaction composition has a pair of primers and fluorescence indicator (See column 32, lines 28-61). It is inherent in this teaching that the nucleic acid sample combined at least one set of reaction compositions comprising a first reaction composition and second reaction composition, both specific for the at least one target polynucleotide, wherein the first reaction composition comprises amplification primers specific to at least one target polynucleotide and the second reaction composition comprises a fluorescent indicator and amplification primers specific to at least one target polynucleotide.

Id.

The Examiner stated that

[t]he response argues that Wittwer et al. fail to disclose the first reaction composition has no fluorescent indicator and the determining step recited as that whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition.

Id. at pages 3-4.

The Examiner then alleged that

[s]ince the method of the instant claims is described by using open language "comprising" to describe the components of the first composition and the method steps, it is inherent that the first composition could have any components to fulfill the method and in the irradiating step, the first composition could be irradiated and in monitoring step the first composition could be monitored.

Id. at page 4. The Examiner maintained the rejection concluding that “based upon the teachings of Wittwer et al. the teachings of Wittwer et al. anticipate the limitations of the claims. . . .” *Id.* The Examiner then suggested “to amend language to exclude a fluorescent indicator used in the first composition, and the first composition, which is not irradiated and monitored for overcoming the 102(e) rejection.” *Id.*

Applicants respectfully disagree that any claim amendment is necessary to obviate the rejection in view of Wittwer in view of at least the reasons of record. Solely to expedite prosecution and without acquiescing to the Examiner’s contentions, however, applicants have amended claim 26 to include the language “the first reaction composition comprises amplification primers specific to the at least one target polynucleotide and lacks a fluorescent indicator.”

Contrary to the Examiner’s suggestion, applicants need not amend claim 26 to recite that the first composition is not irradiated and monitored. Wittwer does not show or suggest, nor has the Examiner contended Wittwer shows or suggests, “a first reaction composition that comprises amplification primers specific to the at least one target polynucleotide and lacks a fluorescent indicator.”

Applicants respectfully assert, as they asserted in the previous responses, that Wittwer does not teach or suggest, either expressly or inherently, “determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition,” according to the method of claim 26, for at least the reasons of record. In addition, Wittwer does not teach or suggest “the first reaction composition comprises amplification primers specific to the at least one target

polynucleotide and lacks a fluorescent indicator.” Therefore, Wittwer does not anticipate claim 26 for at least those reasons, nor does Wittwer anticipate any of claims 28-35, 39, 40, 43-45, and 47-50, which ultimately depend from claim 26. Accordingly, applicants respectfully request reconsideration and withdrawal of the rejection of claims 26, 28-35, 39, 40, 43-45, and 47-50 under 35 U.S.C. § 102(e).

III. Rejection of Claims 27, 36-38, 41, and 42 Under 35 U.S.C. § 103(a)

The Examiner maintained the rejection of claims 27, 36-38, 41, and 42 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wittwer, as applied to claims 26, 28-35, 39, 40, 43-45, and 47-50, and further in view of U.S. Patent No. 6,103,465 (“Johnston-Dow”). Action at page 4, Item no. 2. Applicants respectfully traverse that rejection.

The Examiner acknowledged that “Wittwer et al do not disclose a nucleic acid sequencing reaction on the amplification product, the source of DNA sample used as listed in claims 36-38 and determining at least one HLA type.” *Id.* The Examiner alleged that “Johnston-Dow et al. disclose a method for typing HLA class I gene and the method involving DNA sequencing techniques. . . .” *Id.* The Examiner further alleged that “Johnston-Dow et al. also disclose that any source of human nucleic acid can be used [, and that] Johnston-Dow et al. further indicate that HLA typing is performed routinely in connection with many medical indications. . . .” *Id.* at page 5. The Examiner also alleged that “it would have been prima facie obvious to an ordinary skill in the art at the time of the instant invention to apply the sequencing method of Johnston-Dow et al. because the method of Johnston-Dow et al. is applied to the locus-specific nucleic acid

amplification followed by sequence-specific detection of the amplified product for the DNA typing of HLA class I gene via DNA sequencing. . . .” *Id.* at page 5.

The Examiner stated that

[t]he response argues the same issue as discussed above in connection with claim 26 that “determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition...” As discussed in section 1, with the same reasons as set forth in section 1, the rejection is maintained.

Id. at page 6.

As discussed above in connection with claim 26, applicants have amended claim 26 to include the language “the first reaction composition comprises amplification primers specific to the at least one target polynucleotide and lacks a fluorescent indicator” solely to expedite prosecution and without acquiescing to the Examiner’s contentions. Applicants respectfully assert, as asserted in the previous responses, that Wittwer would not have taught or suggested, either expressly or inherently, “determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition,” according to the method of claim 26, for at least the reasons of record. In addition, Wittwer would not have taught or suggested “the first reaction composition comprises amplification primers specific to the at least one target polynucleotide and lacks a fluorescent indicator,” according to the method of claim 26.

Johnston-Dow would have failed to cure the deficiencies of Wittwer. Specifically, as discussed in the previous responses, Johnston-Dow would have failed to teach or

suggest “determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition . . . ,” according to the method of claim 26. And Johnston-Dow would have failed teach or suggest “the first reaction composition comprises amplification primers specific to the at least one target polynucleotide and lacks a fluorescent indicator,” according to the method of claim 26.

Each of claims 27, 36-38, 41, and 42 ultimately depend from claim 26. Accordingly, Wittwer and Johnston-Dow would not have taught or suggested claims 27, 36-38, 41, and 42. Applicants, therefore, respectfully assert that the Examiner has not established a *prima facie* case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 27, 36-38, 41, and 42 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wittwer in view of Johnston-Dow.

Because claims 27, 36-38, 41, and 42 would not have been obvious for at least the reasons discussed above, applicants do not need to address the Examiner’s contentions concerning other elements of those claims. By not addressing those contentions, applicants in no way acquiesce to those contentions.

IV. Rejection of Claim 46 Under 35 U.S.C. § 103(a)

The Examiner maintained the rejection of claim 46 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wittwer, as applied to claims 26, 28-35, 39, 40, 43-45, and 47-50, and further in view of U.S. Patent No. 6,790,945 (“Lukhtanov”). Action at page 6, item no. 2. Applicants respectfully traverse that rejection.

The Examiner acknowledged that "Wittwer et al. do not disclose using a minor groove binding molecule as a fluorescent indicator." *Id.* at page 6. The Examiner alleged that "Lukhtanov et al. disclose oligonucleotide probes containing a minor groove binding molecule. . . ." *Id.* The Examiner further contended that "[o]ne of ordinary skill in the art at the time of the instant invention would have been motivated to apply the minor groove binding molecule of Lukhta[n]ov et al. because Lukhta[n]ov et al. indicate that the reagents used for labeling oligonucleotide overcome the unfavorable characteristics. . . ." *Id.* The Examiner also alleged that "[i]t would have been prima facie obvious to have minor groove binding molecule as a fluorescent indicator for determining the presence and sequence of at least one target polynucleotide in a sample." *Id.*

The Examiner stated that

[t]he response argues the same issue as discussed above in connection with claim 26 that 'determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition . . . ' As discussed in section 1 above, with the same reasons as set forth in section 1, the rejection is maintained.

Id. at page 7.

Applicants respectfully traverse that rejection. As discussed above in connection with claim 26, applicants have amended claim 26 to include the language "the first reaction composition comprises amplification primers specific to the at least one target polynucleotide and lacks a fluorescent indicator" solely to expedite prosecution and without acquiescing to the Examiner's contentions. Applicants respectfully assert, as asserted in the previous responses, that Wittwer would not have taught or suggested,

either expressly or inherently, “determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition,” according to the method of claim 26, for at least the reasons of record. In addition, Wittwer would not have taught or suggested “the first reaction composition comprises amplification primers specific to the at least one target polynucleotide and lacks a fluorescent indicator,” according to the method of claim 26.

Lukhtanov would have failed to cure the deficiencies of Wittwer. Specifically, as discussed in the previous responses, Lukhtanov would have failed to teach or suggest “determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition . . . ,” according to the method of claim 26. And Lukhtanov would have failed to teach or suggest “the first reaction composition comprises amplification primers specific to the at least one target polynucleotide and lacks a fluorescent indicator,” according to the method of claim 26.

Claim 46 ultimately depends from claim 26. Therefore, Wittwer and Lukhtanov would not have taught or suggested all of the elements of claim 46. Applicants, therefore, respectfully assert that the Examiner has not established a *prima facie* case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 46 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wittwer in view of Lukhtanov.

Because claim 46 would not have been obvious for at least the reasons discussed above, Applicants do not need to address the Examiner’s contentions

concerning other elements of that claim. By not addressing those contentions, Applicants in no way acquiesce to those contentions.

CONCLUSION

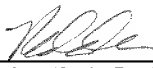
Applicants respectfully request reconsideration of all rejections. Applicants respectfully request the timely issuance of a Notice of Allowance. In the event that the Examiner does not find the claims allowable, Applicants request that the Examiner contact the undersigned at (650) 849-6749 to set up an interview.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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